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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,358	03/01/2006	Koenraad Lodewidjk August Van Acker	TIP0062USPCT	9433

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EXAMINER	
KINSEY, NICOLE	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,358	VAN ACKER ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *15-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/1/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group I (claims 1-14) in the reply filed on July 24, 2007 is acknowledged.

Claim Objections

Claims 1, 5, 6, 7, 9 and 10 are objected to because of the following informalities:

Claims 1, 6, 9 and 10 recite "multi-well." It appears a term is missing after "multi-well." Do applicants mean multi-well plate or multi-well support or multi-well platform?

Claim 5 should recite, "identified as an inhibitor of" instead of "identified at inhibition of."

Claim 7 should recite "according to."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 6, 7, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 refers to Δt in claim 1; however, it is not clear which Δt claim 6 is referring to (Δt of step c or step d).

Claim 7 recites that the assay is "performed under constant reaction conditions including under a CO_2-concentration of 5%, a relative humidity comprised between 95 and 100% and a temperature of 37°C." It is not clear if the conditions after the term "including" are all required to be present or if some of the conditions are required or if the claim is defining what is meant by "constant reaction conditions."

Claim 13 recites the limitation "detectable marker" in reference to claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Kanamoto et al. (Antimicrobial Agents and Chemotherapy, 2001, 45(4):1225–1230) as evidenced by Carrasquillo et al. (Investigative Ophthalmology & Visual Science, January 2003, 44(1):290-299).

The claims are drawn to a multi-well assay for identifying a compound inhibiting the replication cycle of a micro-organism comprising the subsequent steps of:

a) preparing a multi-well comprising micro-organism-coated host cells,

b) initiating at time t micro-organism infection and replication in said micro-organism- coated host cells such that micro-organism infection and replication is initiated synchronically in all host cells,

c) bringing at time t + Δt a candidate compound at one or more concentrations into contact with a part of the host cells,

d) repeating step c) after a time interval of Δt for another part of said host cells,

e) optionally repeating steps c) and d) using one or more other candidate compounds at one or more concentrations, and

f) determining whether said candidate compound has inhibited micro-organism replication in said host cells.

Kanamoto et al. discloses a time-of-addition assay to test the effects of various compounds on HIV replication (see page 1226, Materials and Methods). Kanamoto et al. does not disclose preparing a multi-well plate comprising micro-organism coated host cells. However, it is well known in the art that any time-of-addition assay implicitly requires the use and preparation of multiple assay wells, i.e. a "multi-well." MT4 cells were exposed to HIV at a high multiplicity of infection for 1 hour at 37°C to synchronize the virus replicative cycle in the cells. After 60 min of virus adsorption, the cells were washed to remove unadsorbed viruses. Various compounds were added at 1, 6, 12 15, 18 and 21 hours post-infection. P24 levels were measured to determine if the compound had any affect on HIV replication. As for the culture conditions recited in claim 7, it is well known in the art and routine to culture cells under a CO_2-concentration

of 5 %, a relative humidity between 95% and 100% and at 37°C as evidenced by Carrasquillo et al. (see page 291, Cell Culture under Methods – endothelial cells were grown under standard tissue culture conditions (5% CO2, 37°C, 100% relative humidity)).

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakashima et al. (Biol. Pharm. Bull., 1996, 19:405–412) as evidenced by Carrasquillo et al. (Investigative Ophthalmology & Visual Science, January 2003, 44(1):290-299). Nakashima et al. discloses a time-of-addition assay for identifying a compound that inhibits the replication cycle of a micro-organism (e.g., HIV) (see Abstract). Nakashima et al. performs the assays in microtiter plates. According to Nakashima et al., MT-4 cells were exposed to HIV-1_{IIIB} at a high multiplicity (MOI > 1.0) to ensure that the virus replicative steps were synchronized in the whole-cell population, then incubated for 1 hour at 0°C. After adsorption, the unadsorbed virus was removed by washing 3 times, shifting the temperature to 37°C, and then adding the compounds (e.g., FR901724; 40ug/ml, dextran sulfate; 20ug/ml, AZT; 0.5uM, and KNI-272; 5uM) to parallel cultures in microtiter plates at different times after adsorption or immediately after HIV-I_{IIIB} exposure to MT-4 cells without adsorption. Measuring HIV protein production was used to determine the effect of the candidate compound on HIV replication (see page 407). As for the culture conditions recited in claim 7, it is well known in the art and routine to culture cells under a CO_2-concentration of 5 %, a relative humidity between 95% and 100% and at 37°C as evidenced by Carrasquillo et al. (see page 291, Cell Culture under

Methods – endothelial cells were grown under standard tissue culture conditions (5% CO2, 37°C, 100% relative humidity)).

Claims 1-4, 6-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Fenard et al. (J. Clin. Invest., 1999, 104:611–618) as evidenced by Carrasquillo et al. (Investigative Ophthalmology & Visual Science, January 2003, 44(1):290-299).

Fenard et al. discloses a multi-well assay for identifying a compound that inhibits the replication cycle of a micro-organism (e.g., HIV) (see Figure 2 including the legend). Fenard et al. does not disclose preparing a multi-well plate comprising micro-organism coated host cells. However, it is well known in the art that any time-of-addition assay implicitly requires the use and preparation of multiple assay wells, i.e. a "multi-well." Fenard et al. further discloses initiating at time t micro-organism infection and replication in the micro-organism-coated host cells such that micro-organism infection and replication is synchronized in all host cells (see Figure 2 including the legend - "P4 cells were incubated with virus at 4°C for 90 minutes to allow virus binding. Unbound viruses were then removed by several washes and cells were shifted to 37°C to allow virus entry and infection."). The limitations in steps c) (bringing at time t + Δt a candidate compound at one or more concentrations into contact with a part of the host cells) and d) (repeating step c) after a time interval of Δt for another part of said host cells) are disclosed in Figure 2a including the legend. The limitation of step e) (optionally repeating the two previous steps using one or more other candidate compounds at one or more concentrations) can also be found in Figure 2 including the legend (e.g., AZT).

Fenard et al. also discloses step f) (determining whether said candidate compound has inhibited micro-organism replication in said host cells) in Figure 2 including the legend (the β-gal assay was used to measure the level of viral replication).

The time-of-addition assay of Fenard et al. also included administering the compound at various times during the HIV replication cycle, and the P4 cells contained a detectable marker (β-gal) under the control of the HIV LTR (see page 613, Materials and Methods).

As for the culture conditions recited in claim 7, it is well known in the art and routine to culture cells under a CO_2-concentration of 5 %, a relative humidity between 95% and 100% and at 37°C as evidenced by Carrasquillo et al. (see page 291, Cell Culture under Methods – endothelial cells were grown under standard tissue culture conditions (5% CO2, 37°C, 100% relative humidity)).

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pannecouque et al. (Current Biology, 2002, 12:1169–1177) as evidenced by Carrasquillo et al. (Investigative Ophthalmology & Visual Science, January 2003, 44(1):290-299).

Pannecouque et al. discloses a multi-well assay for identifying a compound that inhibits a particular stage of the replication cycle of a micro-organism (e.g., HIV) (see page 1171-1172 and Figure 2 including the legend). Pannecouque et al. does not disclose preparing a multi-well plate comprising micro-organism coated host cells. However, it is well known in the art that any time-of-addition assay implicitly requires the

use and preparation of multiple assay wells, i.e. a "multi-well." Pannecouque et al. further discloses infecting the cells at time t at a high multiplicity of infection to synchronize all steps of viral replication in host cells (see page 1172). The limitations in steps c) (bringing at time t + Δt a candidate compound at one or more concentrations into contact with a part of the host cells) and d) (repeating step c) after a time interval of Δt for another part of said host cells) are disclosed in Figure 2 including the legend and page 1175. Pannecouque et al. administered compounds such as polyanion, which is known to interfere with binding of the virus to the cell, and AZT and Ritonavir. Pannecouque et al. also discloses step f) (determining whether said candidate compound has inhibited micro-organism replication in said host cells) in Figure 2 including the legend (measure p24 production). As for the culture conditions recited in claim 7, it is well known in the art and routine to culture cells under a CO_2-concentration of 5 %, a relative humidity between 95% and 100% and at 37°C as evidenced by Carrasquillo et al. (see page 291, Cell Culture under Methods – endothelial cells were grown under standard tissue culture conditions (5% CO2, 37°C, 100% relative humidity)).

Claims 1-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Jiang et al. (U.S. Patent No. 7,241,803) as evidenced by Carrasquillo et al. (Investigative Ophthalmology & Visual Science, January 2003, 44(1):290-299).

Jiang et al. discloses a time-of-addition assay to determine whether NB-2 and NB-64 are HIV-1 entry inhibitors. Jiang et al. does not disclose preparing a multi-well

plate comprising micro-organism coated host cells. However, it is well known in the art that any time-of-addition assay implicitly requires the use and preparation of multiple assay wells, i.e. a "multi-well." MT-2 cells were incubated with HIV-1_{IIIB} at 37°C for 0, 1, 2, 3, 4, 6, and 8 hrs, respectively, before addition of the test compounds at 10µg/ml. AZT (2.5µM) was used as a control. After culture for another 2 hrs, the cells were washed to remove the free virus and compounds. The supernatants were collected on day 4 post-infection for measurement of p24 production (see col. 14, line 64 to col. 15, line 12 and FIG. 3). It was determined that NB-2 and NB-64 inhibited HIV by blocking membrane fusion. As for the culture conditions recited in claim 7, it is well known in the art and routine to culture cells under a CO_2-concentration of 5 %, a relative humidity between 95% and 100% and at 37°C as evidenced by Carrasquillo et al. (see page 291, Cell Culture under Methods – endothelial cells were grown under standard tissue culture conditions (5% CO2, 37°C, 100% relative humidity)).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E. Kinsey, Ph.D.
Examiner
Art Unit 1648

/nk/

/Stacy B. Chen/ 10-1-2007
Primary Examiner, TC1600